REMARKS

The Office Action and the cited and applied reference have been carefully reviewed. No claim is allowed. Claims 1, 3-7, 9, 12-17, 21-33, 35-39 and 43-62 presently appear in this application, with claims 24-29, 46-58, 60 and 61 withdrawn from consideration by the examiner, and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The disclosure has been objected to because the examiner alleges that it does not provide sequence identifiers for P1-P2-P3-P4-P5-P6-P7-P8-P9 on page 30 pursuant to 37 CFR 1.821(c) and/or (d). This objection is respectfully traversed.

MPEP 2421.02 states:

> The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. (emphasis added)

The notation P1-P9 merely represents non-specifically define amino acid residues, much like "Xaa", and could equally have been presented as Xaa_1-Xaa_9. As there are no "specifically defined" amino acids in P1-P9, the sequence rules do not embrace the P1-P9 sequence presented on page 30.

Reconsideration and withdrawal of this objection are therefore respectfully requested.

Claims 1, 3, 4, 7, 9 and 12-14 have been rejected under 35 U.S.C. §112, first paragraph, because the examiner states that the specification, while being enabling for the MHC Class I-binding, CTL-inducing peptide epitopes of Table 1, the inventive colo-rectal carcinoma-gene derived peptides in Tables 3 and 5, does not reasonably provide enablement for any peptide isolated from any protein expressed by any polynucleotide from a human colon carcinoma cell where the peptide has the ability to bind MHC Class I and elicit a peptide-specific CTL response and where the peptide optionally includes at least one non-natural modification. This rejection is respectfully traversed.

New claim 62 is directed to an isolated tumor associated antigen (TAA) peptide which does not contain any optional non-natural modification recited in claim 1. Accordingly, at least this rejection is not subject to the issues raised against non-natural modifications.

Regarding the scope of the protein encoded by a polynucleotide overexpressed in human colon carcinoma, Table 2 already provides 26 examples of colorectal-associated genes and a number of HLA-A2.1-restricted peptides identified for each colorectal-associated gene in Table 2. Applicants have used the

three TAA peptides from 1-8D interferon induced transmembrane protein 2 (SEQ ID NO:59) shown to be antigenic and immunogenic in the HHD mouse model (see specification, paragraph [0042]) to provide a working example (paragraphs [00114]-[00118]), where the three 1-8D TAA peptides were shown (1) to induce anti-HCT/HHD CTL response, (2) to be presented on EL4/HHD/1-8D-Myc, (3) to inhibit the growth of HCT/HHD in nude mice with adoptively transferred anti-1-8D peptide lymphocytes, and (4) to activate peripheral CTL precursors in normal human PBMC. Thus, this working example in the specification provides sufficient guidance for one of skill in the art to determine other TAA peptides of a protein encoded by a polynucleotide overexpressed in human colon carcinoma cells that are capable of promoting effective binding to a MHC class I molecule and elicit a CTL response with mere routine experimentation. It would also be well-recognized and appreciated by those of skill in the art that TAA peptides that bind to other types (from different alleles) of HLA class I molecules can be determined in a similar manner to the working example with 1-8D and HLA.A2.1.

Attached hereto are copies of Machlenkin et al., *Cancer Res.* 65:6435-6442 (2005) and *Cancer Immunol. Immunother.* 56:217-226 (2007), Bar-Haim et al., *British J. Cancer* 91:398-407 (2004), Carmon et al., *Int. J. Cancer* and *J. Clin. Invest.* 110(4):453-462

(2002), and Stepensky et al., *Clin. Exp. Immunol.* 143:139-149 (2005), which demonstrate that TAA peptides encoded by prostate cancer-associated genes, bladder transitional cell carcinoma-associated genes or breast cancer-associated genes and binding to HLA.A2.1 and eliciting a CTL response were similarly identified. Those of skill in the art can easily and readily identify TAA peptides from proteins encoded by a polynucleotide overexpressed in human colon carcinoma cells with only routine experimentation given the guidance provided in the present specification and the high skill in the art, as demonstrated by the attached references.

Also attached hereto are post-filing experimental results obtained in the laboratory of the present inventors with a description of the results shown in the figures attached to the description. These results show that some amino acid modifications of 1-8D peptide 3-7 and all tested amino acid modifications of 1-8D peptide 3-5 induced a CTL response.

Regarding non-natural modifications and using positions P1-P9 in paragraph [0062] of the present specification as illustration, paragraph [0063] discloses non-natural amino acid residues for positions P2 and P9. Paragraph [0066] teaches examples of non-natural modifications to the N-terminal residue P1. Paragraphs [0069] and [0070] provide examples of non-natural

modifications where cyclization occurs between positions P4-P8. Accordingly, one of skill in the art is provided direction and guidance in the present specification as to what non-natural modifications can be made at particular positions in the TAA peptide of 8 to 10 amino acid residues.

Applicants submit that the present claims are enabled by the present specification to one of skill in the art.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 15-23 and 30-45 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. This rejection is obviated by the cancellation of claims 18-20, 34 and 40-42 without prejudice and the amendment without prejudice to claims 15-17, 21-23, 30-33, 35-39, and 43-45 to delete the recitation of "pharmaceutical" and "vaccine".

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 5, 6 and 59 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. This rejection is respectfully traversed.

First of all, claim 59 is not directed to TAA peptides but rather to a polypeptide comprising the 132 amino acid

residues of SEQ ID NO:59. It is not understood why claim 59 is subject to this rejection. Furthermore, as disclosed at the bottom of page 18 of the present specification, there are only four nucleotide changes between the encoding nucleotide sequences of SEQ ID NO:60 and SEQ ID NO:58, with the polypeptide of SEQ ID NO:61 being identical to the polypeptide of SEQ ID NO:59 except at residues 41 and 121. Therefore, there is very little difference between SEQ ID NO:59 and SEQ ID NO:61. Moreover, the two residue changes occur outside the three peptides that were identified by binding to HLA.A2 and by eliciting a CTL response. At least with respect to HLA.A2, the TAA peptides in SEQ ID NO:61 would not be expected by different from those obtained from SEQ ID NO:59.

Second, the present specification at page 18 discloses that three peptides 1-6 (SEQ ID NO:11), 3-5 (SEQ ID NO:25) and 3-7 (SEQ ID NO:27), which are also presented in Table 3 on page 49, were identified from the polypeptide encoded by the human 1-8D interferon inducible gene. Paragraph [00224] of the specification teaches that all three 1-8D peptides bind to HLA.A2.1 and induce CTL that specifically lyse HCT/HHD cells. Furthermore, paragraph [00116] discloses that 1-8D peptides are presented by HHD molecules on HCT/HHD cells, paragraph [00117] discloses that adoptively transferred anti-1-8D peptide

lymphocytes inhibit the growth of HCT/HHD in nude mice, and paragraph [00118] discloses that the 1-8D peptides activate peripheral CTL precursors in normal human PBMC. Accordingly, applicants have shown that peptides encoded within nucleotides 31-426 of SEQ ID NO:58 or within SEQ ID NO:60 bind a MHC class I molecule and elicit a CTL response as recited in the claims.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 1, 3, 4, 9 and 12-14 have been rejected under 35 U.S.C. §102(e) as being anticipated by Afar et al., US2005063975. This rejection is obviated by the amendment to claim 1 to exclude STEAP protein. MPEP 2173.05(i) states:

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). (emphasis added)

Accordingly, Afar does not anticipate the present claims. Furthermore, the examiner's statement that STEAP is an 1-89D interferon inducible gene is incorrect. Applicants are unaware of any basis for this assertion.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

In view of the above, the claim comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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